REMARKS

The rejection has been considered at length. However, for the reasons set forth below, it is believed that the claimed subject matter would not have been rendered obvious by the combination of the cited references.

Claims 10-12 and 14-18 are pending and have been examined on the merits.

Claims 10-12 and 14-18 stand rejected under 35 U.S.C. § 103(a) as being obvious over Cavazza (US Patent No. 4,474,812, hereinafter "Cavazza I"), Cavazza (US Patent No. 6,245,378, hereinafter "Cavazza II") and De Felice (US Patent No. 3,830,931, hereinafter "De Felice") in view of De Simone (US Patent No. 6,037,373, hereinafter "De Simone") and Xiu (US Patent No. 6,399,116, hereinafter "Xiu").

Applicants respectfully traverse the rejection.

As previously submitted, the presently claimed invention is directed to a method for treating disorders caused by andropause by administering a combination of propionyl L-carnitine and acetyl L-carnitine. The improvement over the prior art is that the administration of the claimed combination does not increase the level of testosterone in the blood (*e.g.*, page 19, table 11).

Cavazza I does not disclose Applicants' invention. Cavazza I only provides for novel uses of compositions comprising L-carnitine for the treatment of senility (*e.g.*, col. 1, lines 29-33). However, Cavazza I is completely silent with regard to the use of propionyl and acetyl L-carnitines to treat disorders related to andropause without inducing any increase of testosterone blood level.

Cavazza II also suffers from the same deficiencies. Specifically, 'Cavazza II discloses a combination of "carnitines" as the basic active ingredients of a nutritional supplement (*e.g.*, col. 1, lines 9-14). However, as Cavazza I above, Cavazza II is also completely silent with regards to a

method to treat disorders caused by andropause without increasing the blood level of testosterone as claimed herein.

De Felice as well suffers from the same deficiencies of Cavazza I and Cavazza II. Specifically, De Felice only provides for methods for improving myocardial contractility and systolic rhythm by administering carnitine (*e.g.*, col. 1, lines 37-42) and it does not teach the presently claimed method for treating disorders caused by andropause.

De Simone, like De Felice above, does not provide the missing links. De Simone only discloses that carnitines are capable of increasing the level of IGF-1 in human biological fluids (*e.g.*, col. 2, lines 45-55). The increased levels of IGF-1 is useful for the treatment of IGF-1 related diseases such as neuropathies of the optic nerve, neuralgia of the trigeminal nerve, Bell's paralysis, chronic hepatic necrosis etc (*e.g.*, the abstract and col. 4, lines 2-22). Accordingly, De Simone also does not provide any disclosure on a method for treating disorders caused by andropause by administering carnitines without causing an increase in blood level of testosterone.

Finally, Xui provides for administration of a preparation comprising *Rhodiola crenulata* to treat a variety of ailments (*e.g.*, col. 1, lines 5-24). However, Xui describes that one of the activities of *Rhodiola crenulata* comprises a method of increasing testosterone levels in a host in need thereof (*e.g.*, col. 4. lines 43-46). Thus, Xui teaches away from the presently claimed invention which comprises the administration of a composition which does not increase testosterone blood levels. Xui teaches exactly the opposite.

Accordingly, for the reasons set forth above, Applicants respectfully submit that the Examiner's suggested combination would result in a method to administer a composition which would increase the testosterone levels. Thus, the Examiner's statements in this Office Action are incorrect. First, Applicants respectfully disagree with the statement on page 3, lines 1-4 of the

Office Action (*e.g.*, that the limitation of claim 10 drawn to the improvement comprising a lack of increase of blood testosterone is not confirmed). The specification on page 19, Table 11, provides evidence that the limitation of claim 10 is pharmaceutically related to the administration of carnitine as disclosed on page 19, at Table 11.

Specifically, the table shows that upon therapy with testosterone undecanoate the free blood testosterone level increases (from 4.4 to 19.5 pg/ml). On the contrary, the administration of proprionyl L-carnitine and acetyl L-carnitine has no effect whatsoever on the blood level of testosterone (from 4.6 to 4.5 pg/ml). In addition, as for the administration of testosterone, the presently claimed combination does increase the duration of full erections (in minutes) (*e.g.*, page 17, Table 9), but surprisingly does not decrease the level of LH (*e.g.*, page 20, Table 12).

As it is known in the art, testosterone acts as negative feedback on LH levels. Therefore, it is not unexpected that, as shown in table 12, therapy with testosterone leads to a significant decrease of LH blood level. What is unexpected and surprising is that LH level remains unchanged during and after a therapy based upon administration of propionyl and acetyl L-carnitine. Thus, these data demonstrate the unexpected results that the presently claimed method treats the disorders caused by andropause with a mechanism unrelated to the one used by testosterone. This is a substantial and important improvement over the prior art because it is known that treatment with androgens (i.e., testosterone) presents numerous drawbacks.

Applicants also disagree with the comment on page 3, lines 5-9 of the Office Action, related to the "conflict" between claim 10 and claim 11. On page 21 of the present specification, Applicants stated that testosterone resolves the symptoms associated with ageing through a testosterone blood level increase (*e.g.*, Table 12, page 20, as discussed above). Thus, the combination according to the present invention does not present the side effects of the androgen,

because, though acting through a different mechanism (as discussed above) it achieves the same results (*e.g.*, Table 9 and Table 12). This is not in disagreement with the limitation of claim 11, which recites the method of claim 10, further including that andropause is caused by ageing, or, as recited in claim 12, andropause can be caused by surgical or chemical castration.

The subject matter of claim 10-12 is directed to the improvement over the prior art achieved by the combination of propionyl and acetyl L-carnitine, that is, to treat the disorders caused by andropause (which is secondary to many different conditions) without increasing the blood level of testosterone. Thus, claims 10 and 11 are not in conflict.

Applicants also disagree with the comment on page 9, lines 1-7 of the Office Action. Since claim 10 is on a "Jepson claim" format, the difference between the prior art of record and the claim at issue is "a lack of increase of blood testosterone level." The Examiner admits that all of the references are silent with regard to the increase of blood testosterone level with the exception of Xiu. However, this statement is not sufficient to sustain a *prima facie* case of obviousness. As set forth above, the presently claimed subject matter provides an unexpected and surprising result over the prior art. In other words, it provides a method of treating disorders caused by andropause by administering the claimed composition which does not cause any increase in blood testosterone levels. The combination of the cited references does not disclose, teach or even suggest such a method which is not obvious or inherent. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957).

Finally, Applicants assert that the statement that by virtue of their chemical make-up, the carnitines and amino acids are designed as hormone antagonists (*e.g.*, page 9, lines 5-7) is also improper. As discussed above, Applicants respectfully submit that the presently claimed invention achieves the same effect of testosterone, although by an alternative manner. Therefore,

the carnitines do not act as testosterone antagonists at all.

As such, for all of these reasons, it is respectfully submitted that the Examiner's combination of Cavazza I, Cavazza I and De Felice in view of De Simone and Xiu would not have rendered obvious the claimed subject matter to one skilled in the art. Thus, withdrawal of the rejection of claims 10-12 and 14-18 for allegedly being obvious under 35 U.S.C. § 103(a) is respectfully requested.

This response is being filed within the shortened statutory period for response, thus, no fees are believed to be due. If, on the other hand, it is determined that further fees are necessary or any overpayment has been made, the Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. § 1.136(a), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time of its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated herewith is to be charged to the above-mentioned deposit account.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted

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